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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,736	02/24/2000	Mich B. Hein	TSRI-184.2con4	5292

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 08/13/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/512,736	Applicant(s) HEIN ET AL.	
	Examiner Cynthia Collins	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2002 and 31 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-65,67,68 and 70-76* is/are pending in the application.

4a) Of the above claim(s) *21-52,54,55,57-62 and 70-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53, 56, 63-68 and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Amendment filed March 19, 2002, paper no. 11, has been entered. Claim 66 was cancelled. Claims 67-76 were newly added.

The Amendment filed May 31, 2002, paper no. 16, has been entered. Claim 69 was cancelled. Claims 53-65, 67-68, 70-76 were amended.

Claims 53-65, 67-68 and 70-76 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Newly submitted claims 54-55, 57-62 and 70-75 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims either recite that the immunoglobulin product encoded by the nucleotide sequence contained within the plant cell further comprises at least a portion of an immunoglobulin heavy chain, or depend from such claims. The restriction requirement mailed July 5, 2002 set forth three groups of inventions: group I drawn to plant cells containing nucleotide sequences encoding both heavy and light chain immunoglobulin polypeptides, group II drawn to plant cells containing nucleotide sequences encoding heavy chain immunoglobulin polypeptides, and group III drawn to plant cells containing nucleotide sequences encoding light chain immunoglobulin polypeptides. Applicant elected the invention of group III, plant cells containing nucleotide sequences encoding light chain immunoglobulin polypeptides. While claims directed to specific immunoglobulin products comprising an abzyme, a Fab, a Fab', a F(ab')2, an Fv and an antibody were also included in group III and were searched examined in the previous office action, claims

directed to "at least a portion of the variable region of an immunoglobulin heavy chain" were not. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 54-55, 57-62 and 70-75 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 53, 56, 63-68 and 76 are examined on the merits in the instant office action.

Claim Rejections - 35 USC § 112

The previous rejection of claims 53-66 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is withdrawn upon further consideration.

Claims 53, 63-68 and 76 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a nucleotide sequence encoding an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain. The recitation of " at least a portion of the variable region of an immunoglobulin light chain" introduces new subject matter not properly described in the application as filed. The recitation of

" at least a portion of the variable region of an immunoglobulin light chain" encompasses polypeptides having as few as one amino acid to as much as one amino acid less than a full-length polypeptide, yet the original disclosure references antibody fragments that would have been interpreted by one of skill in the art to cover only specific antibody fragments that were known in the art, such as Fab, Fab', F(ab')2 and Fv, not antibody fragments comprising any polypeptide from a single amino acid to one amino acid less than the full length polypeptide. Accordingly, the recitation of " at least a portion of the variable region of an immunoglobulin light chain" is considered an introduction of new subject matter not properly described in the application as filed.

The rejection of claim 53 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "containing" is withdrawn upon further consideration.

Claim 53 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 53 is indefinite in the recitation of "said nucleotide sequences" in part (b). There is insufficient antecedent basis for "nucleotide sequences" in the claim. It is suggested that the claim be amended to recite "nucleotide sequences" in part (a), or "said nucleotide sequence" in part (b).

Claim 53 is also indefinite in the recitation of "said light polypeptide product" in part (b). There is insufficient antecedent basis for " light polypeptide product" in the claim. It is suggested that the claim be amended to recite "said light chain".

Claim 53 is additionally indefinite in the recitation of "derived". It is unclear how much of the light chain is "derived" from the antigen specific immunoglobulin and how much of the light chain is retained by the antigen specific immunoglobulin. It is suggested that the claim recite "obtained" rather than "derived".

Claim Rejections - 35 USC § 102

Claims 53, 56 and 63 remain rejected, and claim 76 is rejected, under 35 U.S.C. 102(b) as being anticipated by During (Dissertation, University of Koln, FRG, July 9, 1988, Applicant's IDS #5), for the reasons of record set forth in the office action mailed November 20, 2001.

Applicant's arguments filed March 19, 2002 have been fully considered but they are not persuasive.

Applicant argues During fails to disclose or teach claim elements including the requirement that the light chain have a leader sequence that forms a secretion signal which is cleaved following proteolytic processing, and the requirement for an antigen specific immunoglobulin product. Applicant further argues that During's insertion of additional amino acids in the vicinity of the leader cleavage site has the potential to adversely influence proteolytic processing of the leader sequence (reply March 19, 2002 pages 10-11). Applicant argues that there was a prejudice in the art against the possibility that plant cells could be used to produce an antigen specific immunoglobulin, and a prejudice in the art against the possibility of using plant cells to process and assemble an antigen specific immunoglobulin, due to the complexity of the native process as it occurs in B cells (reply pages 11-13). Applicant also argues that During's experimental results are internally consistent and lack critical controls (reply March 19, 2002 pages 13-17).

Regarding the requirement that the light chain have a leader sequence which is cleaved following proteolytic processing, the Office notes that the During dissertation teaches an α-amylase leader sequence (page 61) and detection of processed light chain (page 89). That During's insertion of additional amino acids in the vicinity of the leader cleavage site could adversely influence proteolytic processing of the leader sequence is not germane in the absence of evidence that the insertion would have prevented processing. Furthermore, the Office maintains that the expression in a plant cell of a heterologous polypeptide having a leader sequence which is cleaved following proteolytic processing would have been within the abilities of one skilled in the art at the time of Applicant's invention.

Regarding the requirement for an antigen specific immunoglobulin product, the Office notes that the rejected claims require only that the light chain be derived from an antigen-specific immunoglobulin and be capable of forming an antigen-specific immunoglobulin when coexpressed in the same cell with a heavy chain. The anti-NP-IgM antibody taught by During is derived from an antigen-specific immunoglobulin and thus capable of forming an antigen-specific immunoglobulin when coexpressed in the same cell with a heavy chain.

Regarding the assertion of prejudice in the art against the possibility of using plant cells to process and assemble an antigen specific immunoglobulin, the Office notes that the rejected claims are not directed to a processed and assembled antigen specific immunoglobulin.

Regarding the assertion that During's experimental results are internally consistent and lack critical controls, Applicant's arguments and the Lerner declaration are primarily directed to the production of fully assembled antibody molecules in plants, and thus are not commensurate in scope with the claimed invention, which is not limited to fully assembled antibody molecules.

Claims 53, 56, 63-64, 67-68 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by Goodman (US Patent No. 4,956,282, September 11, 1990).

The claims are drawn to a plant cell containing a nucleotide sequence encoding an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain and a leader sequence forming a secretion signal and the immunoglobulin product encoded by said sequence, and to a plant comprising said plant cell.

Goodman teaches transformation of monocot or dicot cells with a DNA construct comprising a mammalian gene of interest, including nucleotide sequences encoding immunoglobulin light chains, and additionally including nucleotide sequences encoding transit or leader sequences that subject the peptide product to processing such as specific peptide cleavage and removal of the transit or leader sequences (column 3 lines 10-23, lines 42-57, column 3 lines 55-64). Goodman also teaches regeneration of transformed plants from said transformed cells (column 5 lines 34-50). Accordingly, claims 53, 56, 63-64, 67-68 and 76 are anticipated by Goodman.

Applicant's arguments filed May 31, 2002 have been fully considered but they are not persuasive.

Applicant argues that Goodman makes only a passing reference to expressing immunoglobulin heavy and light chains together in plant cells, and that the reference is otherwise devoid of teaching for expressing an immunoglobulin in plant cells. Applicant argues that Goodman does not even consider the possibility that light chains may be expressed by themselves, or that such chains can be produced in a manner that allows them to form an antigen specific immunoglobulin when co-expressed in plant cells with the corresponding heavy chain (reply filed May 31, 2002, page 7). Applicant argues that Goodman's success with gamma

interferon is of no significance to the claimed invention because although gamma interferon is a single polypeptide, naturally occurs as a single polypeptide, which does not predict whether or not one can express a single polypeptide that is naturally expressed as a heterodimer, such as an immunoglobulin light chain (reply filed May 31, 2002, page 8).

The Office maintains that the currently rejected claims are not directed to expressing immunoglobulin heavy and light chains together in plant cells, or to producing light chains in a manner that allows them to form an antigen specific immunoglobulin when co-expressed in plant cells with the corresponding heavy chain. The rejected claims are directed to a plant cell containing a nucleotide sequence encoding an immunoglobulin light chain that is capable of forming an antigen specific immunoglobulin when coexpressed in the same cell with a heavy chain. The Office also maintains that Goodman's success with gamma interferon is significant to the claimed invention in that Goodman's success does predict that one skilled in the art can express any single chain mammalian polypeptide in a plant cell, regardless of how it is naturally expressed in a native cell.

Claim Rejections - 35 USC § 103

The rejection of claims 53-64 and 66 under 35 U.S.C. 103(a) as being unpatentable over During (Dissertation, University of Koln, FRG, July 9, 1988, Applicant's IDS #5) in view of Applicant's admitted prior art is withdrawn in light of the amendment of the claims.

Claim 65 remains rejected under 35 U.S.C. 103(a) as being unpatentable over During (Dissertation, University of Koln, FRG, July 9, 1988, Applicant's IDS #5) in view of Applicant's admitted prior art.

Applicant argues that the claims require the light chain to have a leader sequence which is cleaved following proteolytic processing, and that the claims require an antigen specific immunoglobulin product. Applicant further argues that the Lerner declaration demonstrates that there was a prejudice in the art against using plants to produce a processed and assembled immunoglobulin which is antigen specific at the time of the During dissertation, and that During is so lacking in proof that one skilled in the art would not believe During's assertion that plant cells could be used to process and assemble an antigen specific immunoglobulin. Applicant notes that During's work was not published in a peer-reviewed journal until after the inventors' work was published, and asserts that publication of During's work was contingent on the inventors' previous publication. Applicant argues that During is wholly deficient with respect to teaching plant cells containing a nucleic acid encoding an immunoglobulin light chain polypeptide alone, as During attempted and failed to express an immunoglobulin light chain polypeptide by itself. (reply March 19, 2002 pages 19-20).

Regarding the requirement that the light chain have a leader sequence which is cleaved following proteolytic processing, the Office notes that the During dissertation teaches an α-amylase leader sequence (page 61) and detection of processed light chain (page 89) which is cleaved following proteolytic processing. Furthermore, the Office maintains that the expression in a plant cell of a single heterologous polypeptide having a leader sequence which is cleaved following proteolytic processing would have been within the abilities of one skilled in the art at the time of Applicant's invention.

Regarding the requirement for an antigen specific immunoglobulin product, the Office notes that the claims require only that the light chain be derived from an antigen-specific immunoglobulin and be capable of forming an antigen-specific immunoglobulin when

coexpressed in the same cell with a heavy chain. the anti-NP-IgM antibody taught by During is derived from an antigen-specific immunoglobulin and thus would be capable of forming an antigen-specific immunoglobulin when coexpressed in the same cell with a heavy chain.

Regarding the assertion that that there was a prejudice in the art against using plants to produce a processed and assembled immunoglobulin which is antigen specific at the time of the During dissertation, the Office notes that the rejected claims are not limited to plants which produce an assembled immunoglobulin molecule.

Regarding the publication of During's work in a peer-reviewed journal after publication of the inventors' work, the Office maintains that publication of During's work in a peer-reviewed journal is evidence that weighs in support of the enablement of the During dissertation.

Regarding the assertion that During is wholly deficient with respect to teaching plant cells containing a nucleic acid encoding an immunoglobulin light chain polypeptide alone as During failed to detect expression of an immunoglobulin light chain polypeptide by itself, the Office notes that the currently rejected claims are not limited to plant cells containing a nucleic acid encoding an immunoglobulin light chain polypeptide alone. Furthermore, the Office maintains that the assertion that During attempted and failed to express an immunoglobulin light chain polypeptide by itself is not germane to the currently rejected claims because the expression in a plant cell of a single heterologous polypeptide would have been within the abilities of one skilled in the art at the time of Applicant's invention.

Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman (US Patent No. 4,956,282, September 11, 1990) in view of Applicant's admitted prior art.

The claim is drawn to an algal plant cell containing a nucleotide sequence encoding an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain and a leader sequence forming a secretion signal and the immunoglobulin product encoded by said sequence.

The teachings of Goodman are discussed *supra* under 35 USC §102.

Goodman does not teach transformation of an algal plant cell.

While Goodman does not teach transformation of an algal plant cell, at the time of Applicant's invention it would have been well within the means of one of ordinary skill in the art to transform algae with nucleotide sequences such as those taught by Goodman, without any surprising or unexpected results (see, for example, page 27 lines 26-31). Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to transform algae and express a nucleotide sequence encoding an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain and a leader sequence forming a secretion signal, with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Applicant's arguments filed May 31, 2002 have been fully considered but they are not persuasive, for the reasons set forth *supra* under 35 USC §102.

Double Patenting

The rejection of claims 53-66 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-12 of U.S. Patent No. 5,959,177 has been

overcome by Applicant's filing of the Terminal Disclaimer on March 19, 2002, and the rejection is withdrawn.

The rejection of claims 53-66 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,639,947 has been overcome by Applicant's filing of the Terminal Disclaimer on March 19, 2002, and the rejection is withdrawn.

The rejection of claims 53-66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,202,422 has been overcome by Applicant's filing of the Terminal Disclaimer on March 19, 2002, and the rejection is withdrawn.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 53, 56, 63-68 and 76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43-44, 48, 53,

57-59, 79, 81-90 and 93-99 of copending Application No. 09/200657. Although the conflicting claims are not identical, they are not patentably distinct from each other because the plants cells containing a nucleotide sequence encoding an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain of the instant application would encompass the transgenic plants comprising plant cells containing a nucleotide sequence encoding an antigen-specific immunoglobulin single polypeptide product of Application No. 09/200657.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 53, 56, 63-68 and 76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21, 24-40, 43, 50, 54-64, 69 and 80 of copending Application No. 09/512568. Although the conflicting claims are not identical, they are not patentably distinct from each other because the plants cells containing a nucleotide sequence encoding an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain of the instant application would encompass the plant cells containing nucleotide sequences encoding an antigen-specific immunoglobulin of Application No. 09/512568.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 53, 56, 63-68 and 76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 72, 78 and 79

of copending Application No. 09/717888. Although the conflicting claims are not identical, they are not patentably distinct from each other because the plant cell expressing a multimeric protein of Application No. 09/717888 would encompass the plants cells containing an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 53, 56, 63-68 and 76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 86 of copending Application No. 09/982107. Although the conflicting claims are not identical, they are not patentably distinct from each other because the transgenic tobacco plant that comprises nucleotide sequences encoding IgG immunoglobulins of Application No. 09/982107 would be composed of plants cells containing a nucleotide sequence encoding an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
August 9, 2002

James C. Housel 8/9/02
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